

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 16-47, 50-51, 53, and 57-79 are pending in the application. Claims 48-49, 52, and 54-56 are cancelled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejections under 35 U.S.C. § 112***

The Examiner rejected claims 48, 49, 52, 54-46 and 71-77 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have cancelled claims 48, 49, 52, and 54-56. Applicants respectfully traverse this rejection as it applies to the pending claims.

The Examiner stated that

[t]he specification provides no objective evidence to support the assertion that a polynucleotide having 95% sequence identity to SEQ ID NO:1, or a polynucleotide encoding an amino acid sequence having 95% identity to SEQ ID NO:2, or a polynucleotide encoding an amino acid sequence having one to thirty conservative substitutions in SEQ ID NO:2 would correlated [sic] with stage specific breast cancer.

Paper No. 19, page 6.

The Examiner has not provided any reason to doubt the objective truth of the assertion that the claimed polynucleotides are useful in the prognosis of breast cancer.

Clearly, polynucleotides which are 95% identical to a reference polynucleotide, e.g., SEQ ID NO:1, are useful for the detection of the reference polynucleotide. As one of ordinary skill in the art would recognize, the two polynucleotides will hybridize due to the high level of identity between them. The coding sequence of SEQ ID NO:1 is 380 nucleotides long. A polynucleotide which is 95% identical to this sequence would share 361 nucleotides in common with the coding sequence of SEQ ID NO:1, or have up to only 19 nucleotide differences. Thus, a polynucleotide which is 95% identical to SEQ ID NO:1 is useful for detecting expression of SEQ ID NO:1. Expression of SEQ ID NO:1 is correlated with breast cancer prognosis. One of ordinary skill in the art would know how to use the polynucleotides of the claims in breast cancer prognosis by detecting the expression of SEQ ID NO:1.

A patent applicant's specification disclosure which contains a teaching of how to make and use the invention must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *In re Marzocchi*, 439 F.2d. 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). Applicants submit that the Examiner has provided no evidence to doubt the enablement of the claimed polynucleotides. The Examiner has not met his burden in explaining why the skilled artisan would not be enabled to practice the claimed invention throughout the entire scope of the claims.

Additionally, Applicants are not asserting that polypeptides which is 95% identical to SEQ ID NO:2, as encoded by the polynucleotide of claim 76, or a polypeptide with one to 30 substitutions, as encoded by the polynucleotide of claim 72, are, as a whole, overexpressed in breast cancer. Rather, Applicants assert that a polynucleotide encoding such a polypeptide would be useful for detecting SEQ ID NO:1, or, alternatively, would

encode a polypeptide which can raise antibodies which bind to SEQ ID NO:2. In both cases, the polynucleotide would be useful, either directly or indirectly, for detecting breast cancer.

The specification does teach that a polynucleotide with a sequence different from that of SEQ ID NO:1 can still produce a polypeptide which can be used to induce antibodies that bind the protein of SEQ ID NO:2. As the Examiner stated, the specification teaches "polynucleotides comprising nucleic acids which encode fragments of SEQ ID NO:2 from amino acids 94-107 and amino acids 120-127 as antigenic regions of the BCSG1 protein." Paper No. 19, page 3. With this guidance, one of ordinary skill in the art would know which region(s) not to alter in order to obtain a polypeptide which would produce antibodies to SEQ ID NO:2.

The Examiner contends that "even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein." Paper No. 19 at page 6. The Examiner cites two articles in support of her position. However, the two articles cited by the Examiner are directed to studying the effect a mutation has on the biological role of the proteins studied, not on the effect mutations have on the ability to produce antibodies.

It is well established in the art of molecular biology that variants can be routinely made and used in epitope-mapping studies. *See, e.g., Ikeda et al., "Epitope mapping of anti-recA protein IgGs by region specified polymerase chain reaction mutagenesis," J. Biol. Chem.* 267:6291-6296 (1992) (Exhibit A). The experimentation required to make and use such polynucleotides requires little if any ingenuity and, similar to the situation in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988), is merely routine experimentation for one

skilled in the art of molecular biology, especially combined with the teachings of the antigenic regions in the specification.

Applicants assert that the claims are fully enabled, as one of ordinary skill in the art would know how to make and use the polynucleotides of the invention. Accordingly, withdrawal of this rejection is respectfully requested.

***Other Matters***

The Examiner has indicated that the restriction requirement, as applied to claim 79, has been made final. Applicants inform Examiner that a Petition from Requirement for Restriction is being filed herewith.

***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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**Version with markings to show changes made**

Claims 48-49, 52, and 54-56 were cancelled.